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15/63, 5/06, A01K 67/027

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**Published:**  
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10 May 2002

**(72) Inventors; and**

**(75) Inventors/Applicants (for US only):** SCHMITZ, Juer-  
gen [DE/DE]; Josef-Thuener-Strasse 34, 50126 Bergheim

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**(54) Title:** ANTIGEN-BINDING FRAGMENTS SPECIFIC FOR DENDRITIC CELLS, COMPOSITIONS AND METHODS OF USE THEREOF ANTIGENS RECOGNIZED THEREBY AND CELLS OBTAINED THEREBY

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**1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23**

**G3PDH**

## BDCA2

**(57) Abstract:** The invention provides antigen-binding fragments specific for dendritic cells and effective in treatment and/or diagnosing a variety of disorders. Methods of use are also provided as are methods for screening for additional such antigen-binding fragments and the products obtained thereby.

# INTERNATIONAL SEARCH REPORT

International Application No  
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<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C07K16/28 C07K14/705 A61K39/395 G01N33/68 G01N33/50 C12N15/11 C12N15/63 C12N5/06 A01K67/027								
According to International Patent Classification (IPC) or to both national classification and IPC								
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K G01N C12N A01K								
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched								
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, EMBL, WPI Data, PAJ, MEDLINE								
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b> <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>           WO 98 28332 A (TAKASHIMA AKIRA ;UNIV TEXAS (US); ARIIZUMI KIYOSHI (US))            2 July 1998 (1998-07-02)            abstract            page 1, line 13 -page 2, line 12            page 4, line 3-9            page 4, line 27 -page 5, line 2            page 13, line 16-28            page 16, line 3,4            page 73, line 24-26            ---            -/--         </td> <td>           12,27,            31-33,            41-43         </td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	WO 98 28332 A (TAKASHIMA AKIRA ;UNIV TEXAS (US); ARIIZUMI KIYOSHI (US)) 2 July 1998 (1998-07-02) abstract page 1, line 13 -page 2, line 12 page 4, line 3-9 page 4, line 27 -page 5, line 2 page 13, line 16-28 page 16, line 3,4 page 73, line 24-26 --- -/--	12,27, 31-33, 41-43
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.						
X	WO 98 28332 A (TAKASHIMA AKIRA ;UNIV TEXAS (US); ARIIZUMI KIYOSHI (US)) 2 July 1998 (1998-07-02) abstract page 1, line 13 -page 2, line 12 page 4, line 3-9 page 4, line 27 -page 5, line 2 page 13, line 16-28 page 16, line 3,4 page 73, line 24-26 --- -/--	12,27, 31-33, 41-43						
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.								
* Special categories of cited documents : *A* document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filing date *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art *G* document member of the same patent family								
Date of the actual completion of the international search  28 August 2001		Date of mailing of the international search report  12. 09. 01						
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016		Authorized officer  Montrone, M						

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/IB 00/01832

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>RUBARTELLI A ET AL: "The selective engulfment of apoptotic bodies by dendritic cells is mediated by the alpha(v)beta3 integrin and requires intracellular and extracellular calcium"</p> <p>EUROPEAN JOURNAL OF IMMUNOLOGY, DE, WEINHEIM, vol. 27, no. 8, 1 August 1997 (1997-08-01), pages 1893-1900, XP002080456 ISSN: 0014-2980 abstract page 1897, column 2, paragraph 1 -page 1898, column 2, paragraph 2</p>	12,27, 31-33, 41-43, 45,47, 86-89, 95,96
X	<p>LARREGINA A T ET AL: "Pattern of cytokine receptors expressed by human dendritic cells migrated from dermal explants."</p> <p>IMMUNOLOGY, vol. 91, no. 2, 1997, pages 303-313, XP000999720 ISSN: 0019-2805 abstract page 303, column 2, line 1,2 page 304, column 1, paragraph 1 page 305, line 6</p>	12,27, 41-43
X	<p>J VALLADEAU ET AL: "A monoclonal antibody against Langerin, a protein specific of Langerhans cells, is internalized in coated pits and Birbeck granule"</p> <p>JOURNAL OF LEUKOCYTE BIOLOGY, US, FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL, no. SUPPL. 02, 1 October 1998 (1998-10-01), page COMPLETE01 XP002089377 ISSN: 0741-5400 abstract</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	12,27, 41,42

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/IB 00/01832

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>TUTING T ET AL: "Autologous human monocyte-derived dendritic cells genetically modified to express melanoma antigens elicit primary cytotoxic T cell responses in vitro: enhancement by cotransfection of genes encoding the Th1-biasing cytokines IL-12 and IFN-alpha" JOURNAL OF IMMUNOLOGY,US,THE WILLIAMS AND WILKINS CO. BALTIMORE, vol. 160, no. 3, 1 February 1998 (1998-02-01), pages 1139-1147, XP002102051 ISSN: 0022-1767 abstract page 1139, column 1, paragraph 1 -page 1140, column 1, paragraph 2 page 1140, column 2, paragraph 2 page 1146, column 1, paragraphs 2,3</p>	<p>12,27, 41-44, 46,48, 100,101, 108,109, 112-114</p>
X	<p>ROVERE PATRIZIA ET AL: "Dendritic cells preferentially internalized apoptotic cells opsonized by anti-beta2-glycoprotein I antibodies." JOURNAL OF AUTOIMMUNITY, vol. 11, no. 5, October 1998 (1998-10), pages 403-411, XP000996646 ISSN: 0896-8411 abstract page 403, column 1, paragraph 1 -page 404, column 1, paragraph 1</p>	<p>12,27, 41-46, 100,103, 104</p>
X	<p>DATABASE EMBL 'Online! ID: AC006517, 5 February 1999 (1999-02-05) MUZNY D.M. ET AL.: XP002167519 abstract</p>	<p>115-124, 130-133, 135,136, 143-147</p>
X	<p>BROSSART P ET AL: "Virus-mediated delivery of antigenic epitopes into dendritic cells as a means to induce CTL" JOURNAL OF IMMUNOLOGY,US,THE WILLIAMS AND WILKINS CO. BALTIMORE, vol. 155, no. 158, 1997, pages 3270-3276, XP002102050 ISSN: 0022-1767 abstract page 3270, column 1, paragraph 2 -column 2, paragraph 1 page 3271, column 2, paragraph 7 page 3274, column 1, paragraph 2</p>	<p>12,27, 41-44, 46,48, 100,101</p>

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# INTERNATIONAL SEARCH REPORT

International Application No  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	DZIOONEK A ET AL: "BDCA-2, BDCA-3 and BDCA-4: Three novel markers for distinct subsets of dendritic cells in human peripheral blood." TISSUE ANTIGENS, vol. 55, no. Supplement 1, 2000, pages 55-56, XP000999034 7th Workshop and Conference on Human Leucocyte Differentiation Antigens; Harrogate, England, UK; June 20-24, 2000 ISSN: 0001-2815 abstract	1,9,12, 15,27, 31-33, 41,42, 62-64, 71,72, 77,78, 81,83, 100
X	WO 99 21997 A (JOHNSON RICHARD S ; SPRIGGS MELANIE KAY (US); IMMUNEX CORP (US); CO) 6 May 1999 (1999-05-06)  abstract page 2, line 23-33 page 3, line 25-32 page 6, line 14-18 page 13, line 7-36 page 14, line 18-20 page 17, line 15-40 page 39, line 14-32 page 42, line 5-17	1,12-15, 19-21, 24-26, 37-42, 68-70, 75, 77-81, 85,93, 96,100, 103,104, 108-110, 148-152
X	ENGELS FRIEDERIKE H C ET AL: "Calcium signaling induces acquisition of dendritic cell characteristics in chronic myelogenous leukemia myeloid progenitor cells." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 96, no. 18, 31 August 1999 (1999-08-31), pages 10332-10337, XP000999140 Aug. 31, 1999 ISSN: 0027-8424 abstract page 10332, column 2, paragraphs 1-3 page 10333, column 1, paragraph 3 page 10335, column 1, paragraphs 2-4 page 10336, column 1, paragraph 1 -column 2, paragraph 1 page 10337, column 1, paragraph 2	1,86-88, 95,96, 100,108, 109,111

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/IB 00/01832

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIU ET AL: "THE ENHANCING EFFECT OF CALCIUM IONOPHORE A23187 ON THE ACCESSORY FUNCTION OF MOUSE DENDRITIC CELLS" CHEMICAL ABSTRACTS, XP002047046 abstract	86,95
X	THEODORU I ET AL: "CD1 STIMULATION OF HUMAN T CELL LINES INDUCES A RAPID INCREASE IN THE INTRACELLULAR FREE CALCIUM ION CONCENTRATION AND THE PRODUCTION OF IL-2" JOURNAL OF IMMUNOLOGY, vol. 144, no. 7, 1990, pages 2518-2523, XP000996465 ISSN: 0022-1767 abstract page 2518, column 1, paragraph 1 page 2518, column 2, paragraph 3 page 2519, column 2, paragraphs 3-5; table II page 2522, column 2, paragraph 2	1,15, 26-30, 42,43, 45-47, 93,94
X	EVERSON M P ET AL: "Dendritic cells regulate Th1 versus Th3 responses." JOURNAL OF LEUKOCYTE BIOLOGY, no. SUPPL., 1993, page 72 XP001021015 International Congress on the Regulation of Leukocyte Production and Immune Function held at the Joint Meeting of the Australasian Society for Immunology and Society for Leukocyte Biology; Sydney, New South Wales, Australia; December 1-5, 1993 ISSN: 0741-5400 abstract	86-91
X	BAGOT M ET AL: "CD101 is expressed by skin dendritic cells: Role in T-lymphocyte activation." TISSUE ANTIGENS, vol. 50, no. 5, 1997, pages 439-448, XP000999746 ISSN: 0001-2815 abstract page 440, column 1, paragraph 1 page 441; table 1 page 442; figure 3	1,15,19, 20, 25-30, 41,42, 59-61, 81,82, 93,94, 111

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## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/IB 00/01832

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DE SAINT-VIS B ET AL: "The cytokine profile expressed by human dendritic cells is dependent on cell subtype and mode of activation"</p> <p>JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO. BALTIMORE, US, vol. 160, no. 4, 15 February 1998 (1998-02-15), pages 1666-1676, XP002111249 ISSN: 0022-1767</p> <p>abstract page 1666, column 1, paragraph 1 -page 1667, column 2, paragraph 1 page 1673, column 2, paragraph 2 page 1674, column 1, paragraph 4 -column 2, paragraph 3</p> <p>---</p>	<p>1, 15, 19, 20, 25-33, 37-43, 46, 47, 62-64, 68-70, 77-79, 86-90, 95, 96, 111</p>
X	<p>SCHMITT D ET AL: "ANTIGENIC THYMUS-EPIDERMIS RELATIONSHIPS REACTIVITY OF A PANEL OF ANTI-THYMIC CELL MONOCLONAL ANTIBODIES ON HUMAN KERATINOCYTES AND LANGERHANS CELLS"</p> <p>DERMATOLOGICA (BASEL), vol. 175, no. 3, 1987, pages 109-120, XP000999739 ISSN: 0011-9075</p> <p>abstract page 110, column 2, paragraph 4 page 112; table 1 page 115, column 2, paragraph 3 -page 116, column 2, paragraph 1</p> <p>---</p>	<p>1, 15, 27-31, 41, 42, 59-61, 81, 82</p>
X	<p>SOLER P ET AL: "CIGARETTE SMOKING-INDUCED CHANGES IN THE NUMBER AND DIFFERENTIATED STATE OF PULMONARY DENDRITIC CELLS-LANGERHANS CELLS"</p> <p>AMERICAN REVIEW OF RESPIRATORY DISEASE, vol. 139, no. 5, 1989, pages 1112-1117, XP001000305 ISSN: 0003-0805</p> <p>abstract page 1112, column 1, paragraph 2 page 1112, column 3, paragraph 2 page 1113, column 1, paragraph 2</p> <p>---</p> <p style="text-align: center;">-/--</p>	<p>1, 12-15, 19, 20, 25-30, 41, 42, 59-61, 81, 82</p>

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International Application No.

PCT/IB 00/01832

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>LUFT T. ET AL: "Type I IFNs enhance the terminal differentiation of dendritic cells"</p> <p>J. IMMUNOL., vol. 161, 1998, pages 1947-1953, XP002175665</p> <p>abstract page 1947, column 1, paragraph 1 -column 2, paragraph 2 page 1948, column 1, paragraph 3 page 1948, column 2, paragraph 5 page 1952, column 1, paragraph 2 -column 2, paragraph 3</p>	<p>1,12-15, 19,20, 25-27, 31-33, 37-44, 46,47, 62-64, 68-70, 77-80, 86-92, 95-97, 100,101, 103,108, 109,111</p>
X	<p>FITZGERALD-BOCARSLY P ET AL: "VIRALLY-RESPONSIVE IFN-ALPHA PRODUCING CELLS IN HUMAN BLOOD AND TONSIL ARE CD11C/CD123+ CELLS IDENTICAL TO PRECURSORS OF TYPE TWO DENDRITIC CELLS (PDC2)"</p> <p>JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, MARY ANN LIEBERT, NEW YORK, NY, US, vol. 19, no. SUPPL 1, September 1999 (1999-09), page S117 XP001000060 ISSN: 1079-9907 abstract</p>	<p>1,12-20, 25-27, 31-33, 37-42, 86-88, 95-97</p>



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB 00/01832

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 95 to 109, 111 to 114 and 148 to 153 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1(partially), 2 to 4, 9, 12(partially),  
 15 to 27(all partially), 31 to 33,  
 41 to 48(all partially), 49 to 58, 62 to 64, 71,  
 72, 77 to 81 (all partially), 83, 93(partially),  
 94(partially), 98 to 110(all partially),  
 112 to 114(all partially), 115 to 147,  
 148 to 152(all partially), 153,154

Antibodies AC144, AD5-13A11, AD5-4B8 all directed against BDCA-2, BDCA-2 protein and nucleic acid, dendritic cells isolated with said antibodies, methods for isolating said cells using said antibodies, methods for enumerating cells using said antibodies, method of treatments using said cells, recombinant vectors and host cells for said vectors, BDCA-2 antisense molecules.

2. Claims: 1(partially), 6, 7, 10, 11, 12(partially),  
 15 to 27(all partially), 34 to 36,  
 41 to 48(all partially), 65 to 67, 73, 74,  
 77 to 81 (all partially), 84, 93(partially),  
 94(partially), 98 to 110(all partially),  
 112 to 114(all partially),  
 148 to 152(all partially)

Antibodies AD5-5E8, AD5-14H12 all directed against BDCA-3, BDCA-3 protein, dendritic cells isolated with said antibodies, methods for isolating said cells using said antibodies, methods for enumerating cells using said antibodies, method of treatments using said cells.

3. Claims: 1(partially), 5, 12(partially), 13, 14,  
 15 to 26(all partially), 37 to 40,  
 41 to 48(all partially), 68 to 70, 75, 76,  
 77 to 81 (all partially), 85, 93(partially),  
 94(partially), 98 to 110(all partially),  
 112 to 114(all partially),  
 148 to 152(all partially)

Antibody AD5-17F6 directed against BDCA-4, dendritic cells isolated with said antibody, methods for isolating said cells using said antibody, methods for enumerating cells using said antibody, method of treatments using said cells.

4. Claims: 1(partially), 8, 12(partially),  
 15 to 27(all partially), 28 to 30,  
 41 to 48(all partially), 59 to 61, 81 (partially),

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

82, 93(partially), 94(partially),  
98 to 110(all partially),  
112 to 114(all partially)

Antibody AD5-8E7 directed against BDCA-1, dendritic cells  
isolated with said antibody, methods for isolating said  
cells using said antibody, methods for enumerating cells  
using said antibody, method of treatments using said cells.

5. Claims: 86 to 92, 95 to 97, 111

A method of modulating immune capacity of dendritic cells.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 00/01832

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9828332 A	02-07-1998	US 6046158 A	04-04-2000
		AU 5805698 A	17-07-1998
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